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(54) Abstract Title
Control of centrifugal evaporation to prevent bumping

(57) A method of controlling a centrifugal evaporator comprises sensing the temperature of a main chamber 12 of the evaporator prior to the centrifuging of sample materials in solution and comparing this temperature with a stored temperature value. If the sensed temperature is greater than the stored value, a warning signal is generated. The stored temperature value may be directly related to known data on the most volatile of the solutions to be centrifuged such that the stored value may be set at a level that warns of likely bumping / rapid evaporation of this solution past the stored temperature level. Also disclosed is an apparatus associated with the method, comprising a rotatable rotor 18 with drive means 20, a temperature and pressure controlled vacuum chamber 12, temperature sensor 30, data storage means 52, a look up table, and computer means 26 for executing the comparison process, and which generates the warning signal in the event that the sensed temperature exceeds a desired value. The warning signal may be audible or visual and may inhibit operation of the centrifuge. The signal may stop power to the rotor drive 20 or initiate cooling of the chamber. The look up table may be used as a reference for a user to manually enter solution data into the data storage means 52.

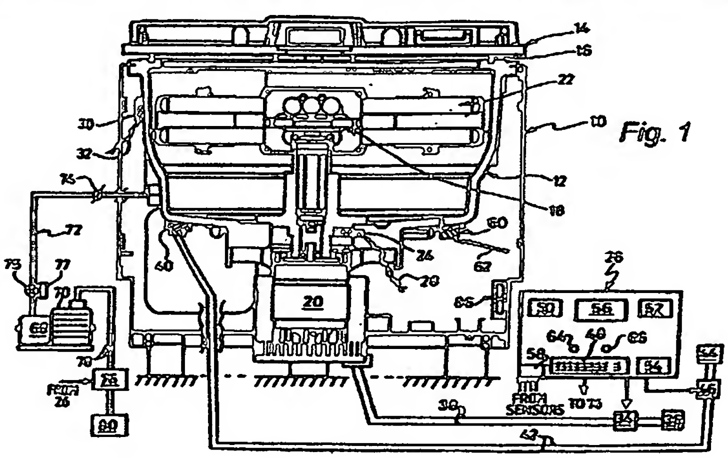

Fig. 1

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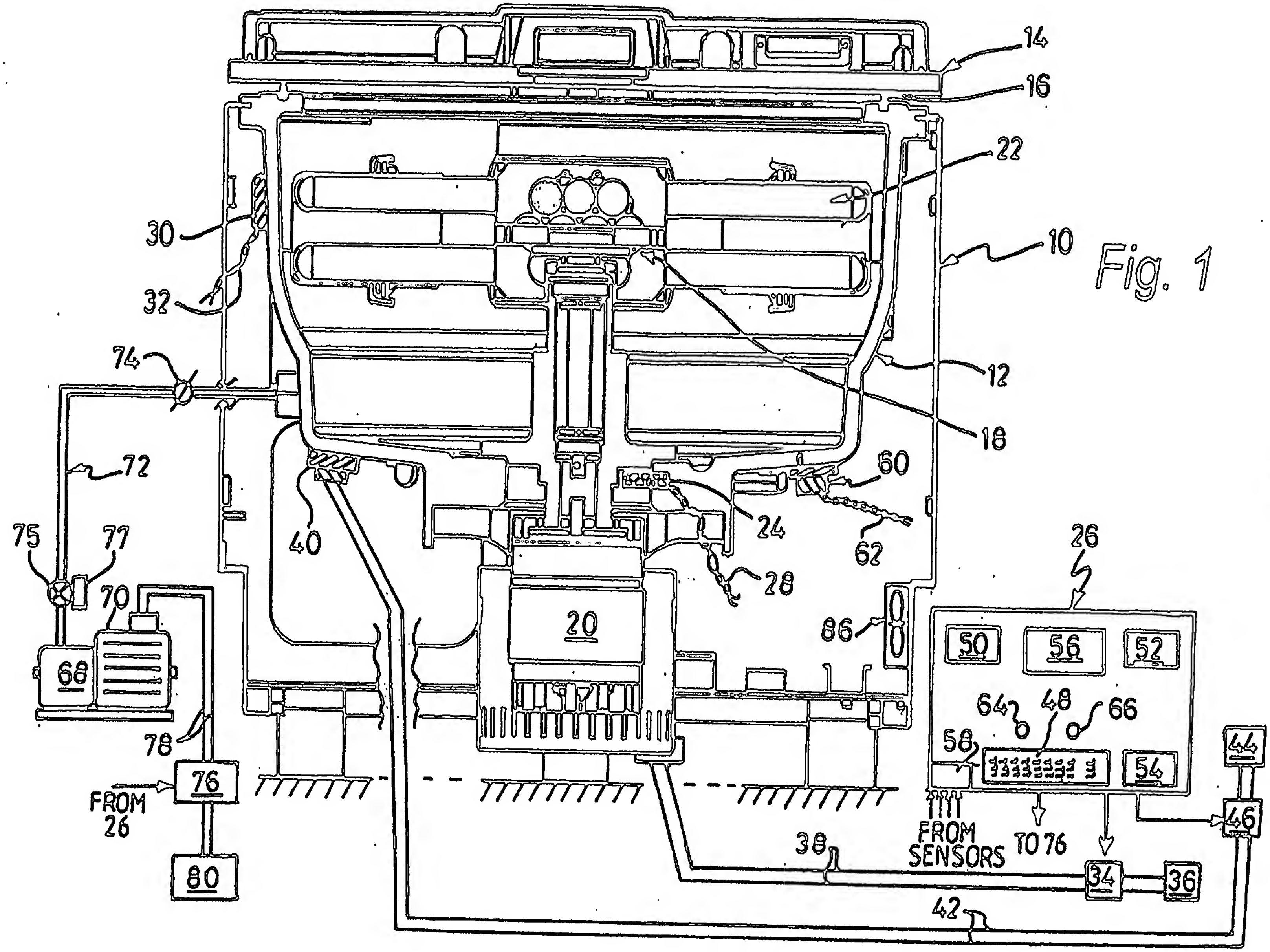
14
16
22
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18
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72
75
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68
78
76
FROM 26
80
40
20
24
28
60
62
86
26
50
56
52
64
48
66
58
54
44
46
FROM SENSORS
TO 76
38
34
36
42

Fig. 1

CONTROL SCHEMATIC

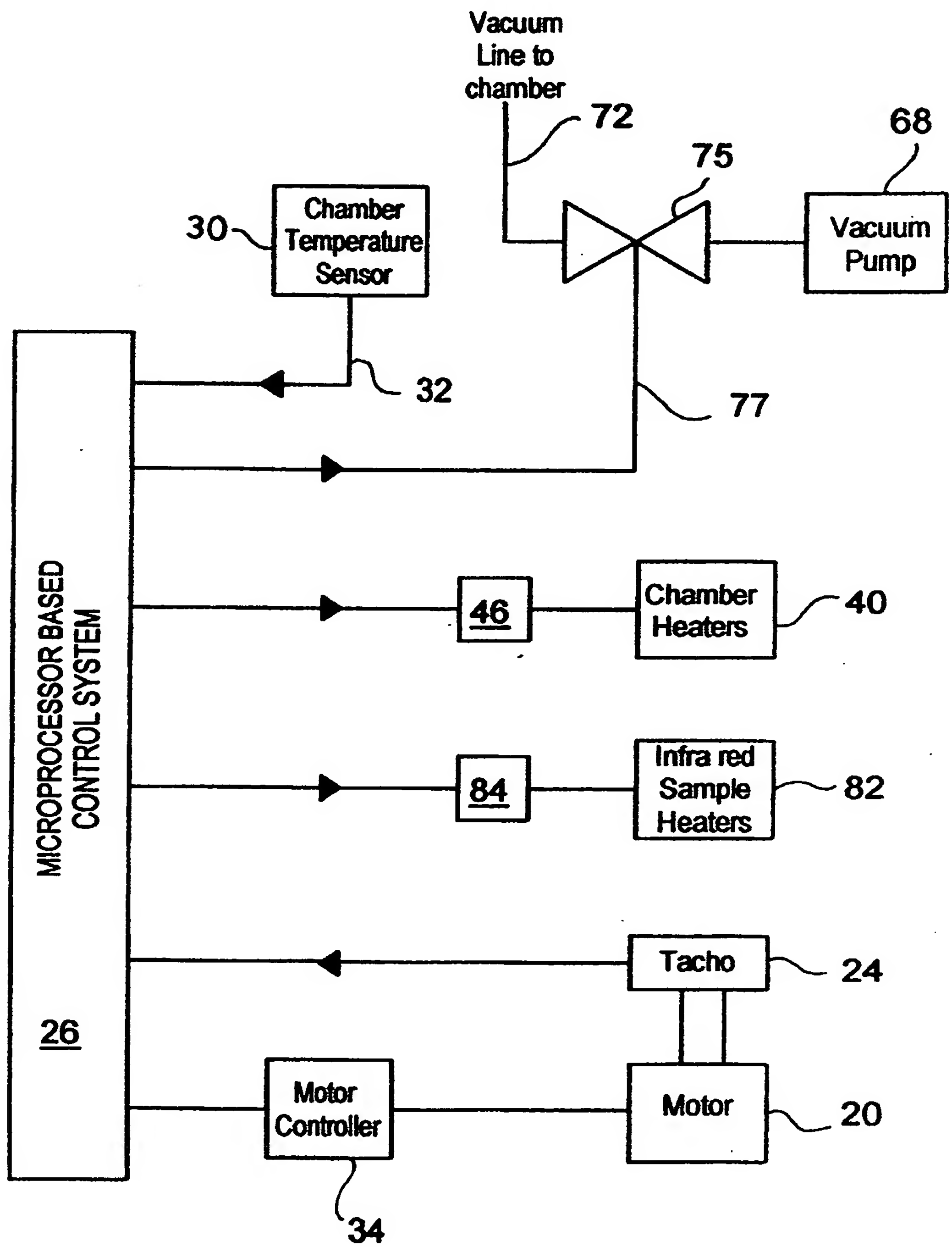

Fig. 2

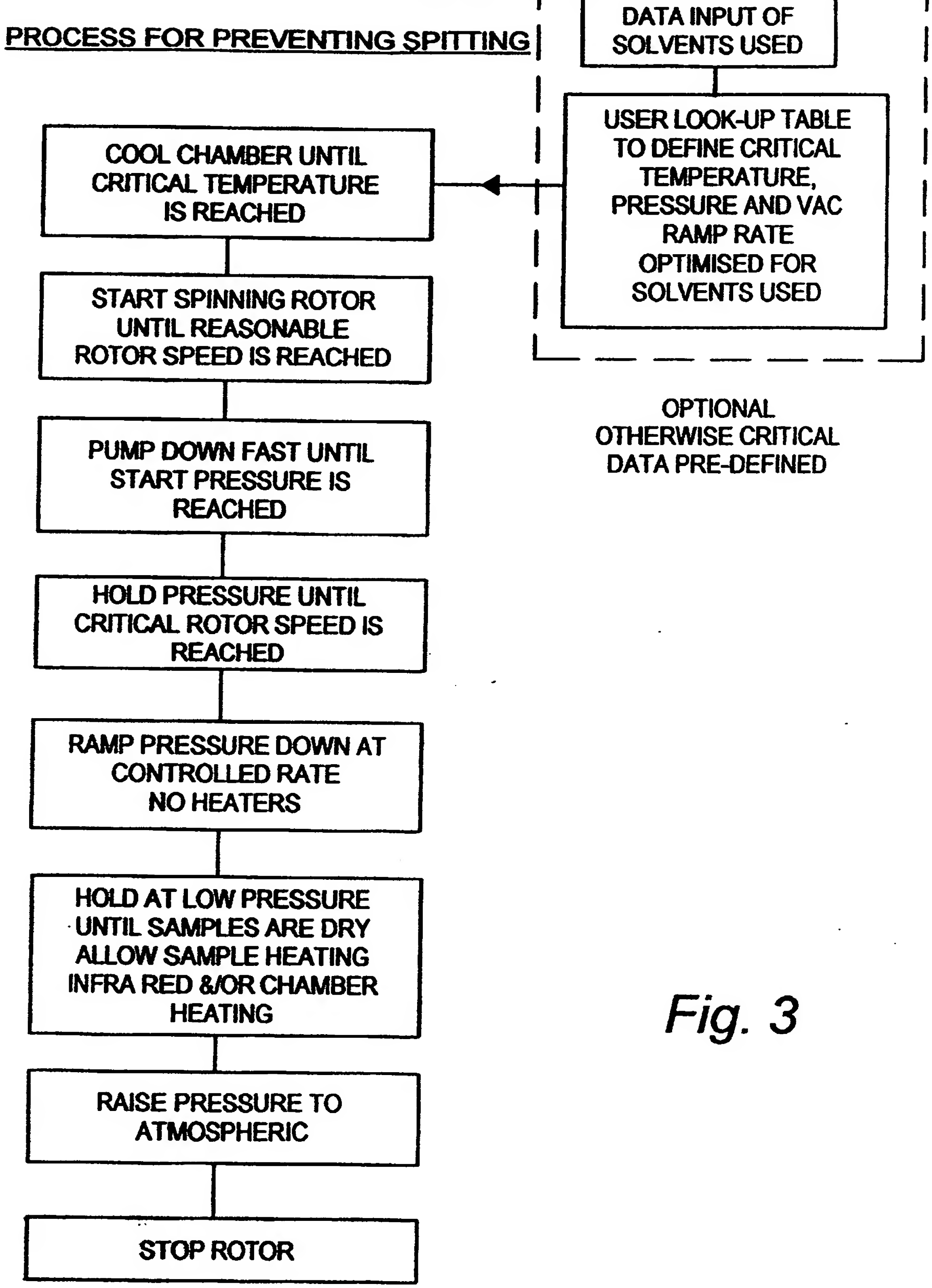
PROCESS FOR PREVENTING SPITTING
DATA INPUT OF SOLVENTS USED
USER LOOK-UP TABLE TO DEFINE CRITICAL TEMPERATURE, PRESSURE AND VAC RAMP RATE OPTIMISED FOR SOLVENTS USED
OPTIONAL OTHERWISE CRITICAL DATA PRE-DEFINED
COOL CHAMBER UNTIL CRITICAL TEMPERATURE IS REACHED
START SPINNING ROTOR UNTIL REASONABLE ROTOR SPEED IS REACHED
PUMP DOWN FAST UNTIL START PRESSURE IS REACHED
HOLD PRESSURE UNTIL CRITICAL ROTOR SPEED IS REACHED
RAMP PRESSURE DOWN AT CONTROLLED RATE NO HEATERS
HOLD AT LOW PRESSURE UNTIL SAMPLES ARE DRY ALLOW SAMPLE HEATING INFRA RED &OR CHAMBER HEATING
RAISE PRESSURE TO ATMOSPHERIC
STOP ROTOR

Fig. 3

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Title: Improved centrifugal evaporator

Field of the invention

This invention concerns centrifugal evaporators and a modification thereto which assists in preventing so called "bumping" during evaporation thereby to reduce the unwelcome effects of cross contamination which can occur if bumping is not prevented.

Background

Centrifugal concentration has been known and widely used for several decades as a means for drying solutions and suspensions of compounds or other solids in liquids. Liquids are boiled at reduced pressures at which the boiling point is low enough to prevent thermal decomposition of the solid sample. The creation of a sufficient g force acting down the axis of the sample tubes can prevent bumping. Typically liquids were water or one of a number of simple organic solvents, and laboratory scale equipment has been available for this purpose for many years. It was generally accepted that 150 – 250g was sufficient centrifugal force to prevent bumping during evaporation and equipment has generally provided this level of centrifugal force, and has often also provided means for heating the walls of the evaporation chamber to provide the heat required to change a solvent from its liquid phase to its vapour phase (the latent heat of evaporation).

In the mid 1990s many pharmaceutical research laboratories started using mixtures of solvents, and some users complained that they were getting sample loss and cross contamination between test tubes during evaporation when using certain solvent mixes, especially mixtures containing Dichlomethane (DCM) and methanol. Investigation revealed

that the inside surface of vacuum chambers in which the samples were being spun were often coated with solid matter and further investigation revealed that this was due to "bumping" caused by a hitherto unknown effect.

Thus with mixtures of a heavy volatile liquid such as DCM (boiling point 40°C at STP and density 1.22 gm/ml) and a less volatile and lighter liquid such as Methanol (boiling point 80°C and density 0.8) the liquids were completely miscible and therefore of even composition before application of vacuum. During evaporation, however, the DCM component was evaporated faster than the methanol so that the surface at which the evaporation was taking place became richer in Methanol and therefore lighter (less dense) than the original mixture. This mixture needed either a higher temperature or lower pressure to achieve the original evaporation rate and in practice a lower pressure option was invariably elected. The pressure therefore became considerably lower than that required to boil the original mixture in the bulk of the liquid. This material was, however covered with a layer of less volatile material that prevented the boiling of the bulk liquid so that the bulk liquid became superheated, and as is known the formation of a nucleus in a superheated liquid causes very vigorous boiling which can result in ejection of vapour and liquid through the methanol-rich blanket, often in such a way that it will leave the container tube at high speed.

Bumping in these solvent mixtures can be prevented by the application of a much higher g force in combination with a controlled ramping of the vacuum. It has been found that a force as high as 450 g is necessary. The ramping of the vacuum is necessary to control the superheating of the solvent. The characteristics of the solvent together with its temperature dictate the critical pressure within the chamber. The critical pressure is the minimum pressure at which the higher g force must be achieved and at which the controlled ramping of pressure must start (i.e. the start pressure). The start pressure is therefore defined by the temperature and physical properties of the most volatile component of the solvent mixture.

If a centrifugal evaporator is in operation under conditions where the rotor has been spinning for a few minutes yet the pressure within the chamber and the temperature of the

solvent are maintained such that the solvent is not boiling, the temperature of the solvent can be assumed to be close to the mean temperature of the evaporation chamber itself. Measuring the chamber temperature under these conditions will give a good indication of the temperature condition of the solvent. This statement is true because with atmospheric pressure within the chamber together with good mixing of the air due to the spinning of the rotor, the rate of heat transfer between the chamber walls and the sample holders is high. In addition, it is in general a requirement of the design of sample holders for use within modern centrifugal evaporators that there is an efficient transfer of heat between the sample holders and the solvent.

The most volatile solvent in common usage within centrifugal evaporation systems is Dichlomethane (DCM), whose boiling point is 40°C at STP. If maintained at 20°C, DCM will start to boil at approximately 450 mbar. If maintained at 35°C, DCM will boil at approximately 850 mbar. Clearly from these figures, the "start pressure" is highly sensitive to the solvent temperature, which in turn can be derived from, and is affected by, the chamber temperature.

One possible solution would be to design a centrifugal evaporator so that the "start pressure" is atmospheric pressure. However this would necessitate a motor and drive train capable of maintaining a rotor speed giving a 450 g acceleration in air at atmospheric pressure within the chamber. The pressure ramp would be designed to ramp from atmospheric pressure at a rate of ramp chosen to prevent excessive superheating of the most volatile component of the solvent mixture. This approach generates a number of problems: 1) a very powerful motor and drive train would be required to generate a 450 g acceleration if the chamber pressure is at atmospheric rather than at 500 mbar. Typically the rotor/chamber combination would require a drive train capable of producing more than twice the torque than would be required at 500 mbar. 2) The air resistance generated at atmospheric pressure relative to that generated at 500 mbar will generate significant and unwanted heating of the solvent. This may necessitate cooling of the chamber as is common practice with laboratory centrifuges. 3) Ramping pressure from atmosphere requires approximately twice as long as compared to ramping from a pressure of 500

mbar. This can be very significant. A typical ramp rate is 11 mbar per minute so a ramp from atmospheric pressure would take approximately one and a half hours to complete.

Summary of the invention

According to the present invention in a method of controlling a centrifugal evaporator to prevent bumping and therefore cross contamination, by using a combination of higher accelerations and controlled ramping of pressure, temperature within the chamber is sensed and a warning signal is generated if the sensed temperature is greater than a stored temperature value associated with the most volatile solvent component present in the chamber.

Where the rotor drive train is sized to achieve a rotor speed equivalent to 450 g at a chamber pressure of approximately half an atmosphere, a suitable pressure ramp is one in which the start pressure is not less than the saturated vapour pressure of the most volatile component of the solvent mixture. The temperature signal derived from the evaporating chamber can be used in a variety of ways.

The warning signal may simply provide a warning to an operator (audible or visible) if the sensed temperature is above a safe value given the most volatile solvent component present, but with no inhibition of operation.

Alternatively an interlock may be provided, such that if a warning signal is generated the power may be prevented from reaching the rotor drive motor until the sensed temperature drops below the safe value.

The method may include the step of force-cooling the chamber in the event that a warning signal is generated, whether the drive motor power is inhibited or not. Thus a fan or thermo-electric cooling element may be operated or the chamber may be associated with a cooling coil connected to a refrigeration unit, which is caused to operate if a warning signal is generated.

Preferably a data entry is provided and the method involves the entering of data by an operator, thereby to key in the solvents or mixtures of solvents in use, which are then compared with a look-up table defining safe temperatures for different solvents or solvent mixures, so as to identify the safe temperature at which evacuation can begin for any given solvent or mixture thereof.

In addition to the safe temperatures, the look-up table may store specific ramp rates for specific solvents or solvent mixtures, and the method involves the utilisation of the particular ramp-rate for the given solvent(s).

The rotor drive may be started automatically as soon as the safe temperature is reached, but alternatively, as a safety feature, automatic start-up may be prevented if a warning signal has been generated, and logic may be provided to generate a second, different, warning signal once the sensed temperature has dropped to a "safe" value, to advise an operator that it is now safe to start the centrifuge.

In addition a rotor speed sensing device and a second interlock may be provided, and the method includes the step of generating a rotor speed signal whose value depends on the rotor speed, and the interlock serves to prevent the centrifuge control system from reducing the chamber pressure below the start pressure unless and until the rotor speed has achieved the speed required to achieve a particular g force, typically 450 g.

Where forced cooling and automatic start-up is provided, the invention allows a pre-used and still hot centrifuge to become active once again in minimum time, whilst guaranteeing that no bumping will occur during pressure ramping.

The invention also lies in apparatus for centrifugally evaporating samples comprising solvent mixtures in a temperature controlled vacuum chamber in which means is provided for reducing the chamber pressure below atmospheric in a controlled manner, means is provided to sense temperature within the chamber, and data storage means is provided for

storing data relating to at least the safe start temperature of at least the more volatile solvent present in the sample or samples in the chamber, and computer based control means is provided to which signals relating to at least the sensed temperature are supplied and by which signals are generated to control operation of the apparatus which is also adapted to generate a warning signal if the sensed temperature is greater than the safe start temperature stored in the data storage means for the more volatile solvent present.

The apparatus may also include interlock means by which power to the rotor drive is inhibited until the sensed temperature drops below the safe start temperature value provided from the data storage means.

The data storage means may be adapted to store the safe start temperature for each of a plurality of different volatile solvents (or solvent mixtures) and means may be provided for selecting the appropriate solvent from a list of options, so as to provide an appropriate safe start temperature value for determining if the sensed temperature is above or below a safe temperature at which the rotor can be spun and the vacuum ramping can be begun.

The apparatus may include means by which data relating to additional volatile solvents and their safe start temperatures may be entered.

The apparatus may include data entry means by which the various solvents known to be present in any batch of samples can be entered and logic is provided for determining the lowest safe start temperature from the data stored in the apparatus, given the solvents indicated as being present.

The apparatus may include a further interlock which prevents the power from automatically being supplied to the rotor drive if and when the sensed temperature is equal to or below the safe temperature, but instead causes a second warning signal to be generated to advise an operator that the apparatus is now safe to start, so that the supply of power to the rotor is under the control of the operator.

Means for sensing the chamber pressure and rotor speed may also be provided, and the control means is adapted to inhibit pressure reduction of the chamber unless the rotor speed is at least equal to a particular stored value.

The data storage means may also include provision to store other data relevant to the different solvents/solvent mixtures such as the ramp rate for the reduction of pressure in the chamber.

Heating and/or cooling means may be provided, which may be activated during the ramp down process and/or before operation of the rotor drive, to adjust the thermal conditions in the chamber as appropriate and data may be stored in relation to different solvents or solvent mixtures to enable logic to determine if and when operation of the heating and/or cooling means is required.

The interlocks and logic may be performed in software stored in a memory or firmware or a combination of both. Data may be stored in a re-writable memory. Basic operational software may be stored in the same or a separate memory for controlling the operation of the computer based control system which serves to provide control signals, warning signals, and to receive and decode temperature and speed and pressure signals from appropriate sensors associated with the chamber and rotor and/or samples.

If sample temperature can be monitored directly or indirectly, then a signal indicative of sample temperature may be employed as the sensed temperature. Alternatively a signal relating to the chamber temperature may be employed as the sensed temperature. Therefore, references to chamber temperature herein are to be understood to include sample temperature.

Typically the start temperature for typical volatile solvents is in the region of 25°C.

The invention will now be described by way of example with reference to the accompanying drawings in which:

Fig 1 is a diagrammatic side elevation of an evaporating centrifuge,

Fig 2 is a schematic diagram showing how the centrifuge is controlled, and

Fig 3 is a logic schematic showing how the centrifuge is controlled at different points in an evaporation procedure and before the latter can start.

Fig 1 shows an evaporating centrifuge the important parts of which are the outer casing 10, and a chamber 12 within the casing which is sealable by a lid 14. A seal 16 ensures that air cannot enter or leave the chamber when the lid is closed.

Within the chamber 12 is rotatably mounted a rotor 18 drive for which is provided by an electric motor 20. The rotor carries a number of sample tubes, one of which is denoted by 22, which adopt a horizontal attitude when the rotor spins, but when stationary pivot into an approximately vertical position. Rotation creates a g force on the tubes and their contents, and by mounting the tubes so that their closed ends are outermost when the rotor spins, the g force acting on the liquid contents of the tubes retains the liquid in the tubes near the closed ends thereof.

A tacho 24 provides a speed signal to a computer based control system 26 via an appropriate connection 28 and a temperature sensor 30 provides a temperature signal along a connection 32, also to the control system 26.

Power to the motor 20 is controlled by the control system which controls the opening and closing of a circuit breaker 34 to control the supply of operating current to the motor from a power supply 36 via leads 38.

A heater 40 is provided for heating the chamber and therefore the sample tubes and their contents and power is supplied to the heater along leads 42. Current flow to the heater

from a power supply 44 is controlled by a circuit breaker 46, in turn controlled by the control system 26.

Depending on the nature of the heater 40 and temperature sensor 30 thermally conductive windows may be provided in the wall of the chamber for the heater and the sensor.

The control system includes a data entry keyboard 48, a processor 50, memory 52, data carrier receptor 54 such as for example a floppy disc port, CD-reader or port into which a solid state memory device can be plugged. A VDU screen 56 allows data and/or status to be displayed to an operator such as indications of operating status, speed, temperature, vacuum pressure (within the chamber), evaporation program (if different programs are available), time to end of current program, solvent(s) in the sample tubes in the current program (in accordance with what has been entered by the operator) and an indication of any fault or hazard conditions and the like.

A suitable interface 58 is provided for digitising the signals from the sensors and in order to provide a measure of chamber pressure a pressure sensor such as 60 is provided and pressure signals are supplied via a connection 62. The signals from the sensors are therefore supplied to the control system bus via the interface 58.

A basic software operating system is loaded into the memory 52 to control the operation of the processor 50 and the transfer of data to and from the bus in a conventional manner. A different part of the memory serves to store semi-permanent data in the form of a look-up table to allow an appropriate program to be selected from memory depending on the data input into the system by the operator via the keyboard 48 such as what solvent(s) is/are present.

When the control system has been appropriately programmed, the samples loaded and the lid closed on the chamber an evaporation process is initiated by keying in appropriate instructions using the keyboard or if provided, by pressing a start button 64.